Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the Claims

1. (Currently Amended) A method for detecting at least one single nucleotide polymorphism in at least one patient nucleic acid containing sample using an electronically addressable microchip having a plurality of test sites, wherein each test site comprises an individually controllable electrode covered by a permeation layer, the method comprising:

[[i.]] (i) providing a plurality of sample nucleic acids from the at least one patient, wherein each sample nucleic acid contains a target nucleic acid sequence containing a different single nucleotide polymorphism locus; ~~at least one sample nucleic acid containing at least one target nucleic acid sequence of interest that contains at least one single nucleotide polymorphism locus;~~

[[ii.]] (ii) electronically biasing one or more specified test sites on the microchip in order to concentrate the plurality of sample nucleic acids at the one or more specified test sites; ~~acid at the specified test sites;~~

[[iii.]] (iii) immobilizing the plurality of sample nucleic ~~acid~~ acids onto the test sites;

[[iv.]] (iv) electronically hybridizing a mixture comprising first and second differently labeled nucleic acid probes to the immobilized plurality of sample nucleic acids ~~acid~~ to form ~~hybridized~~ hybridization complexes, wherein the first probe contains a

sequence specific for one allele of the single nucleotide polymorphism of the locus, and the second probe contains a sequence differing from the first sequence by a single base;

[[v.]] (v) performing electronic stringency on said ~~hybridized~~ hybridization complexes to destabilize hybridization complexes comprising at least one mismatch between the immobilized sample nucleic acid and the hybridized probe; [[and]]

[[vi.]] (vi) detecting hybridization complexes that remain following the electronic stringency step (v) by detecting the hybridized labeled probes; and

(vii) monitoring a detectable signal from the hybridization complexes with a monitoring device in real time during various stages of electronic hybridization and electronic stringency in order to determine when the detectable signal from hybridization complexes comprising at least one mismatch is significantly reduced.

2. (Currently Amended) The method of claim 1, further comprising the step of subjecting the plurality of sample nucleic ~~acid~~ acids containing the target nucleic acid sequence in the patient sample to an amplification reaction whereby the amount of sample nucleic acid containing the target nucleic acid sequence is increased.

3. (Original) The method of claim 1 wherein the single nucleotide polymorphism locus is bi-allelic.

4. (Original) The method of claim 1 wherein the single nucleotide polymorphism locus is multi-allelic.

5. (Currently Amended) The method of claim 1, wherein ~~at least one~~ the target nucleic acid sequence of interest is selected from the group consisting of whole or partial naturally occurring nucleic acid sequences encoding (1) mannose binding protein, (2) Fc-gamma receptors, (3) major histocompatibility complex proteins, (4) Interleukin 1β, (5) lymphotoxin, and (6) tumor necrosis factor α.

6. (Original) The method of claim 1 further comprising providing at least one control target nucleic acid, wherein the control target nucleic acid contains a sequence specific for an allele of the single nucleotide polymorphism locus, and wherein the control target nucleic acid is immobilized at a selected test site.

7. (Currently Amended) The method of claim 2, wherein the plurality of sample nucleic ~~acid~~ acids further comprises a biotin moiety, and the sample nucleic acid is immobilized on the selected test sites by a biotin-streptavidin interaction.

8. (Original) The method of claim 1 wherein the electronic stringency step (v) is carried out until the detectable signal from hybridization complexes comprising at least one mismatch between the immobilized target nucleic sequence and the hybridized probe is significantly reduced as compared to the detectable signal from hybridization complexes without any mismatch between the immobilized target nucleic sequence and the hybridized probe.

9. (Original) The method of claim 8 wherein the electronic stringency step (v) is carried out until the detectable signal from hybridization complexes comprising at least one

mismatch between the immobilized target nucleic sequence and the hybridized probe is approximately the same as a background signal.

10. (Canceled)

11. (Currently Amended) The method of ~~claim 10~~ claim 1, wherein a controller for the power level or length of time of the electronic stringency applied in step (v) is functionally connected to a microprocessor which is functionally connected to the monitoring device, whereby the extent of the electronic stringency applied in step (v) is reduced or ceased in response to the detection of a significantly reduced detectable signal.

12. (Original) The method of claim 1 wherein the first and second nucleic acid probes both contain a sequence specific for an allele of the single nucleotide polymorphism locus.

13. (Original) The method of claim 1 wherein the first and second nucleic acid probes are differently labeled with different fluorophores.

14. (Original) The method of claim 13 wherein the different fluorophores are Cy3 and Cy5.

15. (Canceled)

16. (Original) The method of claim 1 wherein a plurality of sample nucleic acids from each patient sample are immobilized on a selected group of test sites, wherein each sample nucleic acid is immobilized on at least one separate test site, and wherein each sample nucleic

acid contains a target nucleic acid sequence containing a different single nucleotide polymorphism locus.

17. (Original) The method of claim 1 wherein a plurality of patient samples are provided and immobilized on the microchip, and wherein sample nucleic acids from each patient sample are immobilized on a different set of selected test sites on the microchip during steps (iv) through (vi).

18. (Original) The method claim 17 wherein said patient sample nucleic acids are sequentially immobilized onto the test sites by repeating steps (ii) and (iii) for each patient sample.

19. (Original) The method of claim 1 wherein step (iv) is repeated with at least one additional mixture of first and second probes.

20. (Original) The method of claim 1 further comprising the steps of:

(a) stripping all hybridized probes from the immobilized sample nucleic acids using a method selected from the group consisting of electronic denaturing, chemical denaturing, thermal denaturing, and combinations thereof; and

(b) repeating steps (iv) through (vi) with at least one additional mixture of first and second probes.

21. (Original) The method of claim 20 wherein the patient's genotype for more than one single nucleotide polymorphism locus is determined from the data gathered in the multiple steps (vi).